SOME OF THE THERAPEUTIC RELATIONS OF THE NERVOUS SYSTEM.

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SOME OF THE THERAPEUTIC RELATIONS OF THE NERVOUS SYSTEM.

THERE is hardly any subject in the whole range of therapeutic study of more importance than the manifold therapeutic relations of the nervous system, and none more difficult. The difficulty lies not only in the complexity of the problems, but in the want of exact data for their solution. I shall not attempt to cover the whole ground, but merely to indicate the bearing of a few familiar phenomena, as an introduction to special and more thorough studies hereafter.

In highly-developed organisms, such as any of the lower mammals, the nervous system is of extreme importance, on account of its functions in governing the processes of organic life and in regulating the exercise of the functions of animal life. Man, in addition to these, has the exquisitely-developed nervous mechanism of the mind, whose states react in so intricate a manner upon bodily conditions. In order to facilitate our present studies, it will be necessary to entirely ignore

the psychical factor; but even so, we have still a complex mechanism, with far-reaching and insufficiently understood relations, to deal with.

In the protozoa, the undifferentiated protoplasm possesses not only *irritability*, or the power of response to stimulus, but also the power of originating action, or *automatism*. As we proceed higher in the scale of development, while irritability is retained by all the cells of the body, automatism becomes more and more restricted, until at last it is almost exclusively lodged in the specialized tissue which we call nervous matter. The other cells normally act only in response to stimulus of nervous origin, which thus becomes the governing power. When, however, in the normal exercise of reproductive function, the ovum, a cell devoid of specialization, is produced, it contains within itself all the potentialities which, having been *e*volved, must have been *in*volved in the primordial *zoon*. Most fundamental of these is the nutritive-automatism. This fact is of importance in studying the processes of inflammation, repair, and neoplasm-building.

The simplest nervous mechanism consists of three parts,—a nerve-cell or ganglion, which receives impressions from without, and transmutes them into impulses of action; an afferent nerve-fibre, which conveys these external impressions *to* the ganglion, and an efferent nerve-fibre, which transmits, *from* the ganglion, the impulse, which, on arriving at the peripheral organ, results in action. A nerve-cell of this description may, however, be itself under the control of other

nerve-cells, which have the power of preventing or inhibiting its action, or of neutralizing the result of that action ; and these inhibitory cells may themselves be under like dominion. Thus, for example, we have the well-known phenomena of reflex action of spinal nerve-cells, as exhibited in the knee-jerk, which, however, is capable of being prevented by the exercise of the will through the cerebral motor mechanism. So, too, in functions which are wholly involuntary, similar phenomena are manifested. Take, for example, the nervous mechanism of heat and temperature reaction, which play so important a part in the maintenance of the life of warm-blooded animals, and which, when disordered by disease, give rise to the phenomena of fever. Heat is produced in the body as the result of certain of the necessary functions of life ; and, also, it is highly probable, for the special purpose of maintaining temperature, by oxidation of a certain (*thermogen* of MacAllister) portion of muscular substance. Some of this heat is, through the agency of the nervous system, converted into work, and has no effect upon the temperature of the body. Some is dissipated by radiation from the skin, and in the secretions and excretions, especially in the expired air. When neither converted into work nor dissipated, however, the heat necessarily raises the body temperature, and this temperature would thus be subject to enormous variations on account of the varying demands of the different organs for work and of the varying nature of the voluntary activities, were it not for a special mechanism which regulates tempera-

ture. This regulation is accomplished in two ways,—by diminishing the production of heat and by increasing heat dissipation. The regulatory mechanism may, therefore, be looked upon as bearing the same relation to the lower nervous mechanisms, which preside over heat-production or heat-loss, as the brain to the spinal cord. Using the word centre in a broad sense, we then have a *thermogenetic* or heat-producing centre, which stimulates all those processes producing heat, and especially the oxidation of thermogen; a *thermolytic* or heat-dissipating centre, which stimulates respiration, the vaso-dilators, and other mechanisms of heat loss; and a *thermotaxic* or heat-regulating centre, which preserves a proper *balance* between these two. The functions of the thermotaxic centre are probably inhibitory in large degree.

Fever heat being one of the most ordinary manifestations of all forms of disease, it is important that its relations with the nervous system be understood, as far as ascertained facts will permit, so that we can correctly apply therapeutic measures to its treatment.

Hughlings Jackson has shown that the order of dissolution in any nervous mechanism is inverse to the order of evolution. In other words, that which is of latest organization yields first; the pyramid topples at its apex before the base is shaken. The latest organized of the nervous mechanisms of heat is evidently the taxic mechanism. This, as Hale White more especially insists upon, is seen not only by observing its entire absence in cold-blooded animals, its less perfect development in the lower forms of mammals,

but also by observations upon infants, whose temperature, it is well known, is subject to great variations from external causes, from internal vegetative processes, and from the emotions. For this reason, too, high temperature in an infant or a child is of less pathological importance than in an adult. Whether heat-production be increased or diminished, in the normal state of affairs temperature is not apt to vary, save within certain well-defined limits, for the reason that the thermotaxic mechanism causes heat-loss to vary in a complementary manner. When, however, the poison of scarlatina, for example, circulating in the blood, comes in contact with the nerve-cells composing the thermotaxic centre, it interferes with their proper performance of function, and the relation between heat-production and heat loss is *unbalanced*. Balance of function constitutes health; unbalancing is an evidence of disease.

How far, however, the phenomena of fever heat are salutary, tending to preserve the organism and destroy the poison, and how far they are in themselves deleterious, is as yet an unsettled question. I am of those who regard moderate fever-heat as beneficial, both in the light of clinical experience and upon the broad application of biologic doctrines. Its organization in the race as a part of the reaction against toxic agents, is, to my mind, *a priori*, proof of its usefulness. To this subject we will recur in another connection.

Take, again, the case of the circulation. This is regulated by a very complicated nervous apparatus, central and peripheral,

with intercorrelating fibres. Undoubtedly the heart-muscle possesses to a certain extent the power of automatic contraction of unstriped muscular fibre, and this power is greatest perhaps in the auricles. But more important is the nervous mechanism. This consists of a peripheral motor apparatus, which, being stimulated by the presence of blood, causes contraction of the muscles; a central apparatus of motion, which also causes contraction under various appropriate stimuli; and a central and perhaps also peripheral apparatus of nutrition, which controls or inhibits the action of the motor ganglia. Further, the activities of the heart must be correlated in a very intimate manner with the activities of the blood-vessels, with the activities of the lungs, with the activities of the digestive and excretory organs, thus requiring an elaborate apparatus of communication or correlation, all of which is furnished by the nervous system; and so in regard to all other functions or organs. The nervous system excites, restrains, controls, and co-ordinates their action.

Thus it is that disease in one organ or tissue is capable of causing an infinite variety of perturbations in organs at a distance. The further removed it is from the periphery, the greater the number of communicating fibres affected by disorder in the nervous system, and therefore the wider the distribution of secondary disturbances; but disturbance at the periphery may, by so-called reflex disturbance of a centre, simulate central disturbance in degree and area of secondary effects.

While thus the intimate connection and wide distribution of nervous tissues render intricate and confusing the phenomena of disease and of recovery, they also help us, by directing our therapy against some central disturbance, to antagonize a number of morbid phenomena with a single remedy.

The points which we have to consider specially in directing our attention to the therapeutic activities of the nerves are, first, *nutrition;* and, secondly, *special function of tissue innervated.* Most of what I have time to say will be confined to the first of these themes.

The body being a congeries of cells, grouped into organs, each cell having, in addition to sustentation of its own life, a certain function to discharge in the economy of the whole, the nutrition of the body depends first upon the nutrition of the cells; while the nutrition of each cell depends upon its being furnished with proper materials therefor through the functional activity of some other cell. Therefore, not only must the nutrition of each cell be provided for, but it must be kept functionally active, in order that it may do its share towards the nourishment of the others. In truth, nutrition ought to be a broad enough term to include not only assimilation (upbuilding of tissue, or *anabolism*), but also the *dis*assimilation (breaking-down of tissue, or *catabolism*, with expulsion of *débris*, or *excretion*), which is a necessary concomitant of the exercise of function. We may, therefore, consider either that every cell is supplied through the nervous system with two sets of impulses,

—anabolic or nutritive and catabolic or functional,—or that the anabolic phase of nutritive power remains with it as an inheritance from the primordial automatism, while the catabolic phase, being coextensive with function, has passed under nervous control. I know of no experiments which are conclusive as to this point. From clinical observation, I should say that in all probability the potentiality of anabolic automatism remains with cells, but that when normal relations prevail, the process is actually under nervous control.

The health of the body as a whole depends upon the proper *quantitative* performance of both sets of activities. But the health of the cell itself depends upon maintenance of the proper rhythm between them, which, in this sense, may be called *qualitative* performance. Undue preponderance of either means disturbance, and disturbance in one part is necessarily the cause of disturbance, greater or less, in all other parts.

The first point to be determined, then, whether in relation to disorder of the whole system or to disease of a particular part, is in which direction the balance of function has been disturbed; whether there is undue preponderance of cell nutrition, building up the individual at the expense of the society, or whether there is undue preponderance of functional activity, breaking down the individual, and in this case, as in all others, with loss rather than gain to the society.

In most acute febrile disorders we find the latter to be the case; in most inflammatory conditions, the former is the case, with cer-

tain modifications to be pointed out; and in a great many cases the phenomena are so involved that, in the present state of knowledge, we cannot pronounce positively. One process may predominate in one part of the organism, the other, in other parts; as, for example, in tumors associated with cachexia and wasting, or in inflammations associated with fever.

We have already seen that in fever the thermotaxic mechanism is in disorder, in most instances probably as the result of a toxic agent circulating in the blood. The control, inhibition, or *anabolic* function is thus diminished; and the thermogenetic mechanism, being unrestrained, produces increased oxidation of thermogen,—that is, *hypercatabolism*. The result is the wasting of tissues, so commonly observed. The tendency to the production of bed-sores upon very slight mechanical pressure is another evidence of this condition.

Graves appreciated these facts from a clinical stand-point, when "he fed fevers;" though there are other circumstances, too, governing the feeding of fevers, beyond the scope of our present study.

What indication for treatment can we derive from this method of viewing pyrexia? First, we must consider more attentively a matter briefly alluded to a short time ago. It is important that disease and recovery should be looked upon as parts of one continuous process.

The distinguishing characteristic of living things is their ability so to adjust themselves to changes in their environment, or so to adjust some of their parts to changes in other

parts, that the general equilibrium may be maintained. This process of adjustment is continuous in every living thing. Just as the balanced action of centripetal and centrifugal forces serves to keep the planets in their orbits, so the balanced action of destructive and constructive forces serves to maintain the even tenor of life and health. Let either predominate, and we have that disturbance, that *unbalanced condition*, called disease; for hypertrophy (overgrowth,—*i.e.*, *excess of construction, hyperanabolism*) is as much a disease as hypotrophy (want of growth) or atrophy (wasting,—*i.e.*, *excess of destruction, hypercatabolism*).

But the inherent tendency of life, confirmed and organized throughout all the ages of evolution, is to restore the disturbed balance of forces. So soon, then, as, from whatever cause, the *balance of function* we call health is disturbed, and the *unbalanced condition* we call disease is originated, the *inherent tendency to restoration* (*vis medicatrix naturæ*) is called into action, *compensatory disturbance* is set up, and its phenomena become commingled with the phenomena of disease.

To learn to separate in his observation the disturbances of disease from the disturbances of recovery is the most important, as it is the most difficult, task of the student of the art of healing. Its accomplishment in many cases is impossible for want of exact knowledge. Still, we may do much towards improving our knowledge by a careful study of the part taken by the nervous system in the production of these phenomena.

It is a doctrine at least as old as Hip-

pocrates that fever is a conservative process. In its most modern form this doctrine represents the high temperature as destructive to micro-organisms. It is also a well-known fact that heat affects the action of certain drugs, and various experiments have recently been undertaken to show that a moderate fever-heat lessens the toxic effects of the chemical poisons produced in the body by pathogenic microbes; but the evidence is, as yet, too uncertain to lay much stress upon.

Much, however, seems to be beyond reasonable doubt.

Heat applied externally is one of the most valuable therapeutic agents in bringing about resolution of non-suppurative localized inflammation, as cellulitis of an extremity, peritonitis, pleuritis, and pneumonitis at certain stages.

Heat externally, and by means of hot drinks, to promote diaphoresis and "bring out the eruption," is often resorted to in sluggish cases of measles and other exanthemata, and, upon success of the measure, alarming symptoms disappear.

Heat externally and hot drinks had often to be applied by me in the recent epidemic of influenza, because of a coldness and want of circulation, associated with a tendency to collapse; and prolonged subnormal temperature was a marked feature in this class of cases. In one case it was the only objective sign of disease detected.

In cases of threatened collapse in various affections with which we have had experience, and in cholera, with which I fortunately have

had no personal experience, we all know or have read of the great value of heat.

On the other hand, experiments have conclusively shown that greater temperatures than any commonly met with in fevers can be borne by animals for long periods, and that many of the evil results attributed to this heat by former observers cannot be confirmed. Clinical experience, too, multiplies the number of patients known to recover from high temperatures and the number of deaths attributed to the depressing effects of heroic doses of antipyretic drugs. These two lines of observation are further coincident with what might reasonably be deduced from the doctrine of natural selection; that the organization of pyrexial tendencies in the race is an evidence of their protective power.

We need, therefore, not hesitate to affirm, even upon this incomplete presentation of evidence, that the pyrexia of fever is, when within limits, an evidence of the tendency to recovery, and is not to be too hastily interfered with.*

The reaction of the organism against the attacks of disease is not always confined, how-

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* In an "analysis of one thousand cases of acute lobar pneumonia treated at the London Hospital between the years 1880 and 1890," Fenwick (*Brit. Med. Journ.*, January 31, 1891) found that those cases presenting an average temperature of about 103° F. were attended with *the minimum of mortality*, "the states of hyperpyrexia and apyrexia corresponding to the maximum of danger to life." It appears, further, that thirty-five per cent. of all the deaths coincided in time with the sudden defervescence in temperature, the only period more fatal than this being that of the height of the fever. In other words, it is extremes only that are to be dreaded.

ever, within the limits necessary to restore equilibrium. If it were, the physician, like Othello, would find his "occupation gone." Whether from greater instability of organization in certain persons, so that dissolutional processes cannot be brought again under control by the inherent forces of the organism, or from whatever reason, we do at times find symptoms indicative of dangers arising from *hyper*pyrexia. I do not think, however, that we can define the limit between salutary pyrexia and dangerous hyperpyrexia by a line on the thermometer. We must be guided by the association of symptoms, and it is very possible that some of these untoward symptoms may be due to the poison of the disease and not to the heat.

They are those, in general, of profound nervous disturbance,—feebleness and irregularity of the action of the heart, dyspnœa and irregular respiration, insomnia or somnolence, delirium or coma vigil, arrest of secretions, and the like.

They indicate loss of control by higher centres, unrestrained, inco-ordinate action of lower centres and of peripheral mechanisms,—complicated as well by loss of functions in parts unsupplied, or supplied imperfectly or perversely, with blood or with the materials upon which to perform function.

These symptoms demand therapeutic intervention, and it is a fact that, in typhoid fever, for example, where they are often most marked, they may be made to disappear by a measure which also reduces temperature; but—and this is the important point of practice—that measure is not one

which directly depresses the nervous apparatus of heat production.

We have seen that high temperature is not an index of increased heat production simply, but of an increase of heat production *relatively* to heat loss. This is an evidence that the thermotaxic centre has been overthrown, or that the ordinary thermotaxic mechanism is inadequate. We, therefore, turn our attention directly to the lower centres. We can reduce temperature by depressing the thermogenetic centre or mechanism, or by stimulating the thermolytic centre or mechanism, or by artificial thermolysis,—namely, abstraction of heat,—the ends aimed at in the two former methods being accomplished by the use of drugs, the latter being carried out by cold bathing, sponging, ice packing, and the like.

We have drugs, such as antipyrin and its congeners, which exercise a powerful effect in reducing temperature, by depressing thermogenesis. If, however, we study closely the effects of these drugs, we find that not only is the reduction of temperature transient, but that it is often accompanied by depression of other functions which are necessary to the preservation of life,—cardiac and respiratory action, disassimilation, tissue respiration, secretion, and excretion. The action of the poison, then, is not confined to the heat-producing centre, but affects nervous centres of organic life in general; and it is, therefore, to be avoided, as a means of reducing temperature simply, save in extreme cases and with great caution, for temporary purposes. We have as yet no safe drug with which to

depress thermogenesis without the risk of affecting other functions injuriously. This method must, therefore, be set aside.*

Thermolysis may be stimulated by opium in appropriate doses (when this drug is not otherwise counterindicated), nitrous ether, the saline diureto-diaphoretics, and other agents acting upon the lungs, kidneys, skin, and vessels. The amount of reduction of temperature which can be thus effected is not marked, and in all but mild cases such measures have only auxiliary utility.

The method of artificial thermolysis, or abstraction of heat by cold sponging, cold bathing, etc., has in its favor clinical experience, and on theoretical grounds can be best defended. It is very probable, too, that the cold acts upon thermogenesis peripherally,—that is, it checks the oxidation of muscular substance without reference to the nervous impulses, and thus opposes hypercatabolism without depressing general vital functions. It acts also reflexly to allay the central ner-

* Quinine and salicylic acid, with their congeners, often reduce temperature safely, but more probably by destroying the disease poison, as specifics in certain diseases, and we must, therefore, exclude them from present consideration. In massive doses and in general cases, as antipyretics simply, they, too, are to be avoided. Phenacetin, acetanilide, and others of the newer drugs are not so dangerous as antipyrin, and all have their legitimate uses; but we are here dealing with broad principles only, not specific details. The dangers attending their use should never be forgotten, as we never forget the dangers attending the use of opium and arsenic. But there seems to be a tendency to use these new poisons of the laboratory empirically, with insufficient indication and without adequate caution.

vous disturbance, and thus tends to restrain abnormal central action without undue depression of normal function as well. In brief, the thermotaxic centre having been deranged and unable to co-ordinate heat-loss with heat-production, the therapeutist steps in to supply the deficiency. He increases the dissipation of heat, with as little disturbance of other functions as possible, and without interfering with that normal reaction of the organism which is so potent a factor in recovery.

In inflammations, we have said, the processes of anabolism are unduly increased. So far as the cells participating in the inflammation are concerned this is undoubtedly true; it is not true as to the organs, for these suffer in nutrition just in proportion as the nutrition of the cells is unduly increased. It is a condition of dissolution of society, the individual flourishing at the expense of the whole. Further, as organs are made up of various tissues, the higher and more specialized tissues are crowded out and destroyed by the abnormal growth of the lower and less specialized tissues; just as in revolution and riot—even justifiable revolution—the higher orders of citizens suffer the most. Thus, with undue preponderance of cell nutrition, cell function is lost, and the whole organism, therefore, suffers a deprivation of nutritive materials.

How is the abnormal cell nutrition of inflammation manifested? By reproduction. Inflammation produces a reversion of organized structures to aggregations of undifferentiated embryonic cells. As the process con-

tinues, the new cells may finally be deprived of nutrition by mechanically cutting off their own blood-supply, and in other ways; and may thus perish, be absorbed, and resolution occur. This is the normal restoration of balance of function. Or they may fall victims to pyogenic organisms, and suppuration take place. This may aid recovery or introduce new dangers, according to the location of the abscess and other points we cannot now consider. It is also to be noted that the *new cells* of (morbid) inflammatory tissue are no longer under nervous control; they are automatic in their nutrition and incoordinate in their activity; and, although derived from the organism containing and sustaining them, are in reality parasites. They are rioters, who, having become anarchists, are public enemies. But the essential characteristic, from our present point of view, is the abnormal nutrition of individual cells. All other phenomena are secondary to this.

The phenomena of inflammation, then, *in so far as they pass the limits of normal reaction*, have occurred in response to an abnormal impulse, which, whatever may be its detailed mechanism, is, in relation to the cells stimulated or let loose from control, of an anabolic nature. If, now, the therapeutist can divert or neutralize the nervous impulse of supernutrition, reproduction does not take place, and inflammatory tissue is not formed. Here we have a possible explanation of a part of the action of opium in controlling inflammations. Opium intercepts the diseased impulse, whether upon its way to the centre or in its transmutation at the centre, and thus averts the abnormal

stimulation of, or the abnormal loss of control over, the anabolic processes. In all probability the reason why codeine has a special advantage over all other of the derivatives of opium in this application is because it most possesses this power. As yet we do not know why it is that drugs should act in this manner or in the other, but if it should be found, as Brunton has suggested, and as seems plausible, that the phenomena of pharmacology are phenomena of wave interference, we should explain this action of codeine by the size or rate of its wave movement.

To show another application of the doctrine here presented for your reflection, let us take an illustration in which we have a deficiency of anabolic impulse, the so-called condition of neurasthenia. These cases are characterized by the absence of definite organic disease, yet there is wasting of tissue and inability for exertion, a vicious circle acting and reacting to keep up both phases of the disorder. Feeding, improving digestion merely, will not suffice. We administer strychnine, a catabolic agent, whose power is, by stimulating organic processes, to promote the breaking down of tissue. We administer oxygen, the great consumer, the *Loge* of science, and arsenic, an agent which probably destroys tissue; and yet, although we have given agents, the action of which is to increase the breaking down of tissue, the net result is that the patient increases in nutrition. The reason is obvious. Health depends upon a proper balance between cell-nutrition and cell-function. The impulse of

nutrition is called forth by the exercise of function, and function is again rendered possible by the rebuilding effected. But, unless function goes on, nutrition cannot take place. Living tissues are not like inanimate matter, capable of indefinite continuance in quiescence. Life is normal life only when both its phases rhythmically alternate. In neurasthenia this is not the case. Its starting-point may have been indigestion, lessening nerve-nutrition ; or too great nervous exertion, leading to exhaustion ; or a combination of causes may have been at work. Impaired nutrition lessens capacity for function. Lessened function reduces nutrition. There is a vicious circle, and we must choose some one point at which to break it. When, by our therapeutic measures, we have restored the functional activities of the cells, we have restored that condition of the cells which sends to the equilibriating or taxic centre the needed impulse of upbuilding, and in response to that restored normal stimulus we have a restoration of proper nutritive activity.

These are but a few sketchy and imperfect illustrations of the influence of the nervous system in and over disease and recovery.

The subject cannot be thoroughly elucidated in anything short of an elaborate treatise. But the little we have seen may induce us to pay more conscious attention to this phase of the therapeutic science, and, as physiology and pathology give us increased and more exact information, to seize upon that information, and use it in the service of the art of healing.